PASSWORD: ** * * * * RECONNECTED TO STN INTERNATIONAL * * * * * * 045 34D SESSION RESUMED IN FILE 'REGISTRY' AT 09:18:49 ON 25 NOV 2003 FILE 'REGISTRY' ENTERED AT 09:18:49 ON 25 NOV 2003 COPYRIGHT (C) 2003 American Chemical Society (ACS) TOTAL COST IN U.S. DOLLARS SINCE FILE ENTRY SESSION FULL ESTIMATED COST 5.42 5.63 => file uspatfull COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION 5.42 5.63 FULL ESTIMATED COST FILE 'USPATFULL' ENTERED AT 09:19:01 ON 25 NOV 2003 CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS) FILE COVERS 1971 TO PATENT PUBLICATION DATE: 25 Nov 2003 (20031125/PD) FILE LAST UPDATED: 25 Nov 2003 (20031125/ED) HIGHEST GRANTED PATENT NUMBER: US6654958 HIGHEST APPLICATION PUBLICATION NUMBER: US2003217401 CA INDEXING IS CURRENT THROUGH 25 Nov 2003 (20031125/UPCA) ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 25 Nov 2003 (20031125/PD) REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2003 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2003 USPAT2 is now available. USPATFULL contains full text of the <<< >>> <<< >>> original, i.e., the earliest published granted patents or <<< applications. USPAT2 contains full text of the latest US >>> <<< publications, starting in 2001, for the inventions covered in >>> USPATFULL. A USPATFULL record contains not only the original <<< >>> published document but also a list of any subsequent <<< >>> >>> publications. The publication number, patent kind code, and <<< >>> publication date for all the US publications for an invention <<< >>> are displayed in the PI (Patent Information) field of USPATFULL <<< >>> records and may be searched in standard search fields, e.g., /PN, <<< <<< >>> /PK, etc. 111 USPATFULL and USPAT2 can be accessed and searched together >>> >>> through the new cluster USPATALL. Type FILE USPATALL to <<< >>> enter this cluster. <<< <<< >>> <<< Use USPATALL when searching terms such as patent assignees, >>> classifications, or claims, that may potentially change from <<< >>> >>> the earliest to the latest publication. <<< This file contains CAS Registry Numbers for easy and accurate substance identification. => s osteoporosis and estrogen 10431 OSTEOPOROSIS 9899 ESTROGEN 2487 OSTEOPOROSIS AND ESTROGEN T.2 => d 12 300-310 ANSWER 300 OF 2487 USPATFULL on STN L2 2003:200910 USPATFULL

AN TI

Drug metabolizing enzymes

Tang, Y. Tom, San Jose, CA, UNITED STATES

Baughn, Mariah R., San Leandro, CA, UNITED STATES

```
Yao, Monique G., Mountain View, CA, UNITED STATES
       Bandman, Olga, Mountain View, CA, UNITED STATES
       Azimzai, Yalda, Castro Valley, CA, UNITED STATES
       Lal, Preeti, Santa Clara, CA, UNITED STATES
       Gandhi, Ameena R., San Francisco, CA, UNITED STATES
       Ring, Huijun Z., Los Altos, CA, UNITED STATES
       Shih, Leo L., Palo Alto, CA, UNITED STATES
       Yang, Junming, San Jose, CA, UNITED STATES
       Policky, Jennifer L., San Jose, CA, UNITED STATES
       Yue, Henry, Sunnyvale, CA, UNITED STATES
       US 2003138895
                          A1
                               20030724
PΤ
       US 2002-182951
                          Α1
                               20020731 (10)
ΑI
       WO 2001-US4423
                               20010208
DT
       Utility
FS
       APPLICATION
LN.CNT 7363
       INCLM: 435/069.100
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       INCLS: 435/183.000; 435/320.100; 435/325.000; 435/006.000; 536/023.200
NCL
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             435/069.100
       NCLS: 435/183.000; 435/320.100; 435/325.000; 435/006.000; 536/023.200
TC
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       ICM: C120001-68
       ICS: C07H021-04; C12N009-00; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 301 OF 2487 USPATFULL on STN
L2
       2003:200826 USPATFULL
ΑN
TΙ
       BioMAP analysis
       Plavec, Ivan, Sunnyvale, CA, UNITED STATES
TN
       Berg, Ellen L., Palo Alto, CA, UNITED STATES
       Butcher, Eugene C., Portola Valley, CA, UNITED STATES
       US 2003138811
                          A1
                                20030724
PΤ
                                20020905 (10)
       US 2002-236558
                          A1
AΤ
       Continuation-in-part of Ser. No. WO 2001-US7190, filed on 6 Mar 2001,
RLI
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                           20000306 (60)
       US 2000-186976P
PRAI
                           20000407 (60)
       US 2000-195672P
DT
       Utility
       APPLICATION
FS
LN.CNT 3389
       INCLM: 435/006.000
INCL
       INCLS: 435/455.000; 435/325.000; 702/020.000
              435/006.000
NCL
       NCLM:
              435/455.000; 435/325.000; 702/020.000
       NCLS:
       [7]
IC
       ICM: C12Q001-68
       ICS: G06F019-00; G01N033-48; G01N033-50; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 302 OF 2487 USPATFULL on STN
       2003:200810 USPATFULL
AN
       Polynucleotide encoding a novel human growth factor with homology to
TТ
       epidermal growth factor, BGS-8, expressed highly in immune tissue
       Wu, Shujian, Langhorne, PA, UNITED STATES
IN
       Lee, Liana M., North Brunswick, NJ, UNITED STATES
       Feder, John N., Belle Mead, NJ, UNITED STATES
       US 2003138795
                          Α1
                                20030724
PΙ
       US 2002-173461
                          A1
                                20020614 (10)
ΑI
       US 2001-298340P
PRAI
                           20010614 (60)
DT
       Utility
       APPLICATION
FS
LN.CNT 13042
```

٠,

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INCLM: 435/006.000
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NCL
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       NCLS: 435/069.100; 435/183.000; 435/320.100; 435/325.000; 536/023.200
IC
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       ICS: C07H021-04; C12N009-00; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 303 OF 2487 USPATFULL on STN
L_2
ΔN
       2003:200443 USPATFULL
       Human tumor necrosis factor receptor-like proteins TR11, TR11SV1, and
ΤI
       TR11SV2
       Ni, Jian, Germantown, MD, UNITED STATES
TN
       Ruben, Steven M., Brookville, MD, UNITED STATES
       Human Genome Sciences, Inc., Rockville, MD, UNITED STATES, 20850 (U.S.
PA
       corporation)
       US 2003138426
                          A1
                               20030724
PΙ
                               20021030 (10)
ΑI
       US 2002-283105
                          A1
       Continuation-in-part of Ser. No. US 2001-915593, filed on 27 Jul 2001,
RLI
       PENDING Continuation-in-part of Ser. No. US 2000-512363, filed on 23 Feb
       2000, GRANTED, Pat. No. US 6503184 Continuation-in-part of Ser. No. US
       1998-176200, filed on 21 Oct 1998, GRANTED, Pat. No. US 6509173
                           20011030 (60)
       US 2001-330757P
PRAI
       US 2000-221577P
                           20000728 (60)
       US 1999-144076P
                           19990716 (60)
       US 1999-134172P
                           19990513 (60)
       US 1999-121648P
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       US 1997-63212P
                           19971021 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 12581
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INCL
       INCLS: 435/007.200; 530/388.260
       NCLM: 424/146.100
NCL
       NCLS: 435/007.200; 530/388.260
IC
       [7]
       ICM: A61K039-395
       ICS: G01N033-53; G01N033-567; C07K016-40
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 304 OF 2487 USPATFULL on STN
L2
ΑN
       2003:200439 USPATFULL
       Antibody inhibitors of GDF-8 and uses thereof
ΤI
       Aghajanian, Jane, Belgrade, ME, UNITED STATES
IN
       Dunham, William J., Belgrade, ME, UNITED STATES LR
       Wolfman, Neil M., Dover, MA, UNITED STATES
       O'Hara, Denise, Reading, MA, UNITED STATES
       Davies, Monique V., Harpswell, MA, UNITED STATES
       Veldman, Geertruida M., Sudbury, MA, UNITED STATES
       Bridges, Kristie Grove, Maynard, MA, UNITED STATES
       Whittemore, Lisa-Anne, East Walpole, MA, UNITED STATES
       Khurana, Tejvir S., Narberth, PA, UNITED STATES
       Bouxsein, Mary L., Brookline, MA, UNITED STATES
                               20030724
PΙ
       US 2003138422
                          A1
                               20020925 (10)
       US 2002-253532
                          A1
ΑI
                           20010926 (60)
PRAI
       US 2001-324528P
DT
       Utility
FS
       APPLICATION
LN.CNT 2606
       INCLM: 424/145.100
INCL
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INCLS: 530/388.240; 435/326.000

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NCL
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       NCLS: 530/388.240; 435/326.000
IC
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       ICM: A61K039-395
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
1.2
     ANSWER 305 OF 2487 USPATFULL on STN
       2003:197132 USPATFULL
AN
       S-adenosyl methionine regulation of metabolic pathways and its use in
TΙ
       diagnosis and therapy
       Schwartz, Dennis E., Redmond, WA, United States
IN
       Vermeulen, Nicolaas M. J., Woodinville, WA, United States
       O'Day, Christine L., Mountlake Terrace, WA, United States
       MediQuest Therapeutics, Inc., Seattle, WA, United States (U.S.
PA
       corporation)
       US 6596701
                          В1
                               20030722
PΤ
       WO 9633703 19961031
       US 1998-930128
                               19980316 (8)
ΑI
                               19960425
       WO 1996-US5799
       Continuation-in-part of Ser. No. US 1995-476447, filed on 7 Jun 1995,
RLI
       now abandoned Continuation-in-part of Ser. No. US 1995-428963, filed on
       25 Apr 1995
       Utility
DТ
       GRANTED
FS
LN.CNT 4938
INCL
       INCLM: 514/046.000
       INCLS: 435/007.100; 528/338.000; 528/340.000
              514/046.000
NCL
       NCLM:
              435/007.100; 528/338.000; 528/340.000
       NCLS:
IC
       [7]
       ICM: A01N043-04
       ICS: G01N033-53; C08G069-26
       435/7.1; 514/46; 528/338; 528/340
EXF
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 306 OF 2487 USPATFULL on STN
1.2
       2003:195048 USPATFULL
ΑN
       PPAR-gamma modulator
TI
       Amemiya, Yoshiya, Yokohama-shi, JAPAN
IN
       Wakabayashi, Kenji, Urayasu-shi, JAPAN
       Takaishi, Sachiko, Ohta-ku, JAPAN
       Fukuda, Chie, Shinagawa-ku, JAPAN
       SANKYO COMPANY, LIMITED, Tokyo, JAPAN (non-U.S. corporation)
PA
                               20030717
PΙ
       US 2003134859
                          A1
                               20021023 (10)
       US 2002-278387
                          A1
ΑI
       Continuation-in-part of Ser. No. WO 2001-JP3655, filed on 26 Apr 2001,
RLI
       UNKNOWN
PRAI
       JP 2000-129565
                           20000428
                           20010305
       JP 2001-60366
DT
       Utility
       APPLICATION
FS
LN.CNT 6541
       INCLM: 514/247.000
INCL
       INCLS: 514/252.010; 514/255.050; 514/255.060; 514/256.000; 514/340.000;
              514/365.000; 514/374.000; 514/375.000; 514/372.000; 514/415.000;
              514/416.000; 514/406.000; 514/619.000; 514/616.000; 514/603.000;
              514/471.000; 514/310.000; 514/314.000; 514/459.000; 514/457.000;
              544/238.000; 544/333.000; 544/295.000; 544/405.000; 546/268.100;
              548/146.000; 548/152.000; 548/217.000; 548/207.000; 548/241.000
              514/247.000
NCL
       NCLM:
              514/252.010; 514/255.050; 514/255.060; 514/256.000; 514/340.000;
       NCLS:
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514/365.000; 514/374.000; 514/375.000; 514/372.000; 514/415.000;
              514/416.000; 514/406.000; 514/619.000; 514/616.000; 514/603.000;
              514/471.000; 514/310.000; 514/314.000; 514/459.000; 514/457.000;
              544/238.000; 544/333.000; 544/295.000; 544/405.000; 546/268.100;
              548/146.000; 548/152.000; 548/217.000; 548/207.000; 548/241.000
IC
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       ICS: A61K031-501; A61K031-497; A61K031-4439; A61K031-427; A61K031-422;
       A61K031-4035; A61K031-404; A61K031-4709; A61K031-366
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 307 OF 2487 USPATFULL on STN
1.2
AN
       2003:195018 USPATFULL
       Halogenated sulphamate-, phosphonate-, thiophosphonate-, sulphonate- and
ΤI
       sulphonamide- compounds as inhibitors of steroid sulphatase
       Reed, Michael John, Sterix Limited, UNITED KINGDOM
TN
       Lloyd Potter, Barry Victor, Sterix Limited, UNITED KINGDOM
       Hejaz, Hatem, Dubai, UNITED ARAB EMIRATES
       Purohit, Atul, Sterix Limited, UNITED KINGDOM
       US 2003134829
                          Α1
                                20030717
PΙ
       US 2002-165599
                          A1
                                20020607 (10)
ΑI
       Continuation-in-part of Ser. No. WO 2000-GB4689, filed on 7 Dec 2000,
RLT
       UNKNOWN
       WO 2001-44268
                            20010621
PRAI
       GB 1999-29445
                            19991213
       GB 2000-4317
                            20000223
                           20000721
       GB 2000-18040
DT
       Utility
FS
       APPLICATION
LN:CNT 2149
       INCLM: 514/177.000
INCL
       INCLS: 552/523.000
NCL
       NCLM: 514/177.000
       NCLS: 552/523.000
       [7]
TC
       ICM: A61K031-56
       ICS: C07J031-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 308 OF 2487 USPATFULL on STN
       2003:195000 USPATFULL
AN
       Methods and compositions comprising hydroxyapatite useful for the
TI
       administration of therapeutic agents
       Jackson, John, Vancouver, CANADA
ΤN
       Springate, Christopher, Vancouver, CANADA
       Wong, Wesley, Vancouver, CANADA
       Burt, Helen M., Vancouver, CANADA
                                20030717
PΙ
       US 2003134811
                          Α1
       US 2002-259277
                                20020926 (10)
                          Α1
ΑI
                            20011009 (60)
       US 2001-328379P
PRAI
                            20011009 (60)
       US 2001-328175P
DT
       Utility
       APPLICATION
FS
LN.CNT 1953
       INCLM: 514/044.000
INCL
       INCLS: 514/449.000; 514/251.000
NCL
       NCLM: 514/044.000
       NCLS: 514/449.000; 514/251.000
IC
       [7]
       ICM: A61K048-00
       ICS: A61K031-525; A61K031-337
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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```
ANSWER 309 OF 2487 USPATFULL on STN
L2
       2003:194999 USPATFULL
AN
       Methods and compositions comprising biocompatible materials useful for
TI
       the administration of therapeutic agents
       Springate, Chris, Vancouver, CANADA
IN
       Jackson, John K., Vancouver, CANADA
       Winternitz, Charles, Delta, CANADA
       Burt, Helen M., Vancouver, CANADA
PΙ
       US 2003134810
                          A1
                               20030717
ΑI
       US 2002-259260
                          A1
                                20020926 (10)
                           20011009 (60)
PRAI
       US 2001-328175P
       US 2001-328203P
                           20011009 (60)
DΥ
       Utility
       APPLICATION
FS
LN.CNT 2217
INCL
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       INCLS: 514/055.000
NCL
       NCLM: 514/044.000
       NCLS: 514/055.000
IC
      . [7]
       TCM: A61K048-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 310 OF 2487 USPATFULL on STN
L2
       2003:194977 USPATFULL
AN
       Human tumor necrosis factor receptor TR16
ΤI
       Baker, Kevin P., Darnestown, MD, UNITED STATES
IN
       Young, Paul E., Gaithersburg, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
                                20030717
ΡI
       US 2003134788
                          Α1
                                20020213 (10)
ΑI
       US 2002-73333
                          Α1
       Continuation-in-part of Ser. No. US 2000-637856, filed on 10 Aug 2000,
RLI
       ABANDONED
                            20010214 (60)
       US 2001-268364P
PRAI
       US 1999-148348P
                            19990812 (60)
                            19990813 (60)
       US 1999-148683P
                            19990816 (60)
       US 1999-148758P
                            19990813 (60)
       US 1999-148870P
                            19990817 (60)
       US 1999-149181P
                            19990818 (60)
       US 1999-149453P
                            19990819 (60)
       US 1999-149498P
       Utility
DT
       APPLICATION
FS
LN.CNT 13800
       INCLM: 514/012.000
INCL
       INCLS: 530/350.000; 536/023.500; 435/069.100; 435/320.100; 435/325.000
       NCLM: 514/012.000
NCL
       NCLS: 530/350.000; 536/023.500; 435/069.100; 435/320.100; 435/325.000
IC
       [7]
       ICM: A61K038-17
       ICS: C07K014-715; C12P021-02; C12N005-06; C07H021-04
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
=> s 11 and pd<1995
             0 L1
       1890748 PD<1995
                 (PD<19950000)
             0 L1 AND PD<1995
L3
=> s 12 and pd<1995
```

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1890748 PD<1995
                 (PD<19950000)
           189 L2 AND PD<1995
=> d 14 179-189 bib, ab, kwic
     ANSWER 179 OF 189 USPATFULL on STN
T.4
AN
       78:63787 USPATFULL
TI
       Antiosteoporotic agents
       Samour, Carlos M., Wellesley, MA, United States
IN
       Vida, Julius A., Greenwich, CT, United States
       Bristol-Myers Company, New York, NY, United States (U.S. corporation)
PΑ
PΙ
       US 4125621
                               19781114
ΑI
       US 1978-866930
                               19780104 (5)
       Division of Ser. No. US 1977-795570, filed on 10 May 1977, now patented,
RLI
       Pat. No. US 4101668
DΤ
       Utility
FS
       Granted
EXNAM Primary Examiner: Friedman, Stanley J.
       Simon, Morton S., Berdo, Robert H.
LREP
       Number of Claims: 8
CLMN
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 431
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       It is disclosed that compounds of the formula: ##STR1## WHEREIN Y
AB
       represents (C.dbd.O).sub.m in which m has a value of 0 or 1; n has a
       value of 0 or 1; and X represents S, NH or O; provided that there is a
       COOH substituent at the 1, 2 or 3 position relative to the X group; and
       further provided that when X is NH and n is 0, the COOH group cannot be
       at the 2 position; or a nontoxic, pharmaceutically acceptable salt
       thereof are capable of decreasing the ratio of the rates of bone
       resorption to bone deposition in a host animal, e.g., in the treatment
       of osteoporosis.
                                                                     <---
       US 4125621
                               19781114
PΙ
       . . . the ratio of the rates of bone resorption to bone deposition in
AR
       a host animal, e.g., in the treatment of osteoporosis.
       Osteoporosis is a common condition in adults which is
SUMM
       evidenced by a decrease in bone density throughout the body. In fact,.
         . more rapid in women than in men. However, after age 80 there is no
       sex difference in the incidence of osteoporosis. In the course
       of 10 to 20 years of bone loss there may be symptoms of back pain and
       X-ray. . . the bones becomes evident by the ease in which the hip
       bone fractures as the result of a simple fall. Osteoporosis is
       the most common cause of fractures in people over age 45.
       Although the cause of osteoporosis is poorly understood, it is
SUMM
       believed that there is an imbalance between bone production and bone
       resorption (bone breakdown). Bone.
SUMM
            . Whedon, Clinical Endocrinology, II, 349-376 (1968)). Moreover,
       it is estimated that there are currently another 10 million persons
       suffering from osteoporosis who have not yet developed
       symptoms. Various types of osteoporosis are designated
       according to special conditions believed to be causative: senile
       (aging); post-menopausal (female loss of estrogenesis); disuse (chronic
       immobilization); steroid (long term steroid treatment as in arthritis).
       Osteoporosis may also be manifested in dental problems since the
       jaw bone appears to lose mass more rapidly than any other bone. Thus,
       periodontal disease involving a loosening of the adult teeth may be an
       early sign of osteoporosis.
       Anabolic agents and estrogen therapy have been the therapy of
SUMM
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choice for osteoporosis in post-menopausal women.

Unfortunately, recent studies have indicated that patients taking

estrogens may have an increased incidence of cancer of. Physical therapy is another method currently used to treat SUMM osteoporosis since immobilization can cause osteoporosis at any age. Thus, many physicians believe that exercise and physical therapy can prevent the progression of the disease in. . . physical therapy can be harmful for patients with fractures and moreover, overstrenuous exercise can cause fractures in patients with severe osteoporosis. . . . which is symptomatic in some elderly patients. There is, SUMM however, no evidence that a higher intake of calcium will prevent osteoporosis or increase bone mass and it could increase urinary calcium excretion. The most promising therapeutic approach to the treatment of SUMM osteoporosis is the administration of agents which have been designed to modify the balance between the rate of bone production and. . . . e.g., bovine, etc., source. Thus, none of the foregoing agents SUMM are at present suitable for use in the treatment of osteoporosis It is an object of this invention to provide a method wherein a host SUMM animal, including man, suffering from osteoporosis is treated in order to modify the balance between the rates of bone deposition and bone resorption in said host. . . . are capable of reducing the relative rate of bone resorption SUMM and are thus useful in, for example, the treatment of osteoporosis. . . . media of other necessary but unknown factors. Therefore, DETD compound 327-9 was tested in vivo for its ability to prevent immobilization osteoporosis. Rats (150-180 g.) were utilized as the subjects in this experiment. The triceps tibial insertion (knee cap tendons) were severed. CLM What is claimed is: 6. A process in accordance with claim 1, wherein said host animal is treated for osteoporosis. ANSWER 180 OF 189 USPATFULL on STN L478:37955 USPATFULL AN Antiosteoporotic agents ΤI Samour, Carlos M., Wellesley, MA, United States IN Vida, Julius A., Greenwich, CT, United States Bristol-Myers Company, New York, NY, United States (U.S. corporation) PA 19780718 US 4101668 PΙ US 1977-795570 19770510 (5) ΑI DTUtility FS Granted EXNAM Primary Examiner: Friedman, Stanley J. Simon, Morton S., Berdo, Robert H. LREP Number of Claims: 10 CLMN ECL Exemplary Claim: 1 No Drawings DRWN LN.CNT 430 CAS INDEXING IS AVAILABLE FOR THIS PATENT. It is disclosed that compounds of the formula: ##STR1## WHEREIN Y AB represents (C.dbd.O).sub.m in which m has a value of 0 or 1; n has a value of 0 or 1; and X represents S, NH or O; provided that there is a COOH substituent at the 1, 2 or 3 position relative to the X group; and further provided that when X is NH and n is O, the COOH group cannot be at the 2 position; and further provided that when n is 0, the carboxyl group is attached to the ring containing the X and Y ring members or a nontoxic, pharmaceutically acceptable salt thereof are capable of

decreasing the ratio of the rates of bone resportion to bone deposition

```
in a host animal, e.g., in the treatment of osteoporosis.
                               19780718
ΡI
       US 4101668
         . . the ratio of the rates of bone resportion to bone deposition in
AB
       a host animal, e.g., in the treatment of osteoporosis.
       Osteoporosis is a common condition in adults which is
SUMM
       evidenced by a decrease in bone density throughout the body. In fact,.
         . more rapid in women than in men. However, after age 80 there is no
       sex difference in the incidence of osteoporosis. In the course
       of 10 to 20 years of bone loss there may be symptoms of back pain and
       X-ray. . . the bones becomes evident by the ease in which the hip
       bone fractures as the result of a simple fall. Osteoporosis is
       the most common cause of fractures in people over age 45.
       Although the cause of osteoporosis is poorly understood, it is
SUMM
       believed that there is an imbalance between bone production and bone
       resorption (bone breakdown). Bone.
       . . Whedon, Clinical Endocrinology, II, 349-376 (1968)). Moreover,
SUMM
       it is estimated that there are currently another 10 million persons
       suffering from osteoporosis who have not yet developed
       symptoms. Various types of osteoporosis are designated
       according to special conditions believed to be causative: senile
       (aging); post-menopausal (female loss of estrogenesis); disuse (chronic
       immobilization); steroid (long term steroid treatment as in arthritis).
       Osteoporosis may also be manifested in dental problems since the
       jaw bone appears to lose mass more rapidly than any other bone. Thus,
       periodontal disease involving a loosening of the adult teeth may be an
       early sign of osteoporosis.
       Anabolic agents and estrogen therapy have been the therapy of
SUMM
       choice for osteoporosis in post-menopausal women.
       Unfortunately, recent studies have indicated that patients taking
       estrogens may have an increased incidence of cancer of.
       Physical therapy is another method currently used to treat
SUMM
       osteoporosis since immobilization can cause osteoporosis
       at any age. Thus, many physicians believe that exercise and physical
       therapy can prevent the progression of the disease in. . . physical
       therapy can be harmful for patients with fractures and moreover,
       overstrenuous exercise can cause fractures in patients with severe
       osteoporosis.
       . . . which is symptomatic in some elderly patients. There is,
SUMM
       however, no evidence that a higher intake of calcium will prevent
       osteoporosis or increase bone mass and it could increase urinary
       calcium excretion.
       The most promising therapeutic approach to the treatment of
SUMM
       osteoporosis is the administration of agents which have been
       designed to modify the balance between the rate of bone production and.
         . . e.g., bovine, etc., source. Thus, none of the foregoing agents
SUMM
       are at present suitable for use in the treatment of osteoporosis
       It is an object of this invention to provide a method wherein a host
SUMM
       animal, including man, suffering from osteoporosis is treated
       in order to modify the balance between the rates of bone deposition and
       bone resorption in said host.
       . . . are capable of reducing the relative rate of bone resorption
SUMM
       and are thus useful in, for example, the treatment of
       osteoporosis.
       . . . media of other necessary but unknown factors. Therefore,
DETD
       compound 327-9 was tested in vivo for its ability to prevent
       immobilization osteoporosis. Rats (150-180 g.) were utilized
       as the subjects in this experiment. The triceps tibial insertion (knee
       cap tendons) were severed.
CLM
       What is claimed is:
       8. A process in accordance with claim 1, wherein said host animal is
```

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ANSWER 181 OF 189 USPATFULL on STN
L4
ΑN
       78:32164 USPATFULL
       Method of treating the symptoms of menopause and osteoporosis
TI
       Benson, Harvey D., Cincinnati, OH, United States
IN
       Grunwell, Joyce Francis, Hamilton, OH, United States
       Johnston, John O'Neal, Cincinnati, OH, United States
       Petrow, Vladimir, Chapel Hill, NC, United States
       Richardson-Merrell Inc., Wilton, CT, United States (U.S. corporation)
PA
                               19780620
PΤ
       US 4096254
                               19770222 (5)
ΑI
       US 1977-770400
       Continuation-in-part of Ser. No. US 1976-684949, filed on 10 May 1976,
RLI
       now abandoned
DТ
       Utility
FS
       Granted
EXNAM Primary Examiner: Roberts, Elbert L.
       Hattan, L. Ruth, Retter, Eugene O., Rauchfuss, Jr., George W.
LREP
       Number of Claims: 18
CLMN
       Exemplary Claim: 1
ECL
DRWN
       No Drawings
LN.CNT 729
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Compounds of the following general formula are useful in treating the
AB
       symptoms of menopause and osteoporosis: ##STR1## wherein R is
       -- CHO or -- CH. sub.2 OR. sub.1; each of R. sub.1 and R. sub.2 is hydrogen,
       alkylcarbonyl wherein the alkyl moiety has from 1 to 20 carbon atoms and
       is straight or branched, benzoyl, phenylalkylcarbonyl wherein the alkyl
       moiety has from 1 to 6 carbon atoms and is straight or branched or
       cycloalkylcarbonyl wherein the cycloalkyl moiety has from 5 to 10 carbon
       atoms; R.sub.3 is hydrogen; or R.sub.2 and R.sub.3 together form a
       double bond between the 17-position carbon atom and the oxygen atom.
       Method of treating the symptoms of menopause and osteoporosis
TI
                               19780620
       US 4096254
PΙ
       Compounds of the following general formula are useful in treating the
AB
       symptoms of menopause and osteoporosis: ##STR1## wherein R is
       -- CHO or -- CH. sub.2 OR. sub.1; each of R. sub.1 and R. sub.2 is hydrogen,
       alkylcarbonyl wherein the alkyl.
       This invention relates to methods of treating the symptoms of menopause
SUMM
       and osteoporosis and pharmaceutical compositions useful for
       said treatment.
       It is believed that the symptoms of menopause are due primarily to
SUMM
       estrogen deficiency since when menopause occurs there is a
       marked decrease in ovarian estrogen production and since the
       administration of estrogens, for example, diethylstibestrol, conjugated
       estrogens or estradiol provide a specific and effective manner. .
       be set against the undoubted benefits resulting from their use. For
       example, diethystilbestrol, a once widely used and well established
       estrogen, has been implicated as possibly being responsible for
       vaginal cancer and adenosis of the female offspring of pregnant women
       treated.
       The present invention provides a novel and improved method of treating
SUMM
       the symptoms of menopause and osteoporosis which comprises
       administering androstene compounds described more fully hereinbelow.
       Some of the compounds employed in the present invention, for example,.
            knowledge, the use of the compounds employed in the present
       invention in the treatment of the symptoms of menopause or
       osteoporosis has not been taught or suggested heretofore.
       This invention relates to a method of treating the symptoms of menopause
SUMM
       and osteoporosis by administering a compound of the following
       general formula: ##STR2## wherein R is -- CHO or -- CH. sub.2 OR. sub.1;
```

```
. . . of the skin, particularly exposed facial skin and a thinning of
DETD
      the epidermis and loss of rete ridges, and post-menopausal
      osteoporosis or osteopenia. Other symptoms of menopause include
      chilling sensations, paresthesias, and muscle cramps. The present
      invention also relates to the treatment of osteoporosis in
      warm blooded animals and mammals for example, dogs, cats, rats, bovine
      cows, horses and humans including but not limited. . . The methods of
      the present invention offer distinct advantages over the usual methods
      of treating the symptoms of menopause and osteoporosis, that
      is, estrogen therapy, in that the compounds employed do not
       result in certain deleterious side effects resulting with
      estrogen therapy as will become more apparent hereinafter.
       . . . compounds as represented by each of general Formulas II and III
DETD
      in the treatment of the symptoms of menopause and osteoporosis
      represent preferred embodiments of this invention. The use in the
      treatment of the symptoms of menopause and osteoporosis of the
       compounds of general Formula III represents a more specifically
      preferred embodiment of this invention. Other embodiments of this.
      of the compounds as represented by general Formulas IV and V in the
      treatment of the symptoms of menopause and osteoporosis with
      the use of the compounds of general Formula IV wherein R.sub.1 and
      R.sub.2 each represent hydrogen and the compounds.
      In the treatment of osteoporosis the compounds employed in the
DETD
      present invention can be administered alone or in the form of
      pharmaceutical preparations to the. . . to be treated and the
      severity of the condition. The effective amount of compound to be
      administered orally in treating osteoporosis in humans will
       vary from about 0.01 mg/kg up to 3.0 mg/kg, and preferable from about
       0.1 mg/kg to 1.0 mg/kg. For parenteral administration the effective
       amount of compound to be administered in treating osteoporosis
       in humans will vary from about 0.01 mg/kg up to 3 mg/kg and preferably
       from 0.1 mg/kg to 1.0 mg/kg. The effective amount of compound to be
       employed in treating osteoporosis in warm blooded animals and
      mammals other than humans will vary from about 0.01 mg/kg to about 30
      mg/kg, preferably. . . 10 mg/kg and most preferably about 0.1 mg/kg
       to 3 mg/kg. As used herein in reference to the treatment of
       osteoporosis the term patient is taken to mean warm blooded
       animals, mammals, for example, dogs, cats, rats, bovine cows, horses and
      humans. Osteoporosis in the art is a recognized bone disorder
       or skeletal disorder associated with loss of hydroxyapatite, that is,
       calcium phosphate.
           . in need thereof in the effective amounts described hereinabove
DETD
       results in the effective treatment of the symptoms of menopause and
       osteoporosis without the occurence of certain deleterious side
       effects reported to occur with the administration of estrogenic agents
       including uterine endometrial.
       Since with the occurrence of menopause there is a marked reduction of
DETD
       ovarian estrogen production resulting in a gap in the
       reproductive hypothalamo-pituitary-ovarian feedback system there is an
       increase in circulating levels of gonadotrophins,.
            . that the compounds employed at the effective dosages enumerated
DETD
       hereinabove do not result in certain deleterious side effects associated
       with estrogen therapy, such as, uterine growth and
       interference with blood clotting mechanisms.
      The data contained in the following Table I indicate that
DETD
       3,17-dioxoandrost-4-en-19-al does not bind in vitro with the
      estrogen receptor of uterine estrogen target tissue.
      This binding is the first step necessary for hormonal action. To obtain
       these data female hamsters were ovariectomized.
                     TABLE 1
DETD
```

Uterine Cytosol Affinity Relative Estrogen Treatment Binding Affinity Estradiol 100 Estrone 22 Estriol 10 3,17-Dioxoandrost-4-en-19-al 0.01 The lack of estrogen binding affinity of 3,17-dioxoandrost-4-DETD en-19-al supports the finding of lack of certain estrogenic side effects of the compounds employed in the. What is claimed is: CLM15. A method of treating osteoporosis in a patient in need thereof which comprises administering to said patient a compound of the formula in an amount effective to treat osteoporosis: ##STR10## wherein R is --CHO or --CH.sub.2 OR.sub.1; each of R.sub.1 and R.sub.2 is hydrogen, alkylcarbonyl wherein the alkyl. . ANSWER 182 OF 189 USPATFULL on STN L4AN 78:13014 USPATFULL TI Method of inducing an estrogenic response Benson, Harvey D., Cincinnati, OH, United States IN Grunwell, Joyce Francis, Hamilton, OH, United States Johnston, John O'Neal, Cincinnati, OH, United States Petrow, Vladimir, Chapel Hill, NC, United States Richardson-Merrell Inc., Wilton, CT, United States (U.S. corporation) PA 19780307 US 4078060 PΙ US 1976-684944 19760510 (5) ΑI Utility DTFS Granted EXNAM Primary Examiner: Roberts, Elbert L. Hattan, L. Ruth, Retter, Eugene O., Rauchfuss, Jr., George W. LREP Number of Claims: 7 CLMN ECL Exemplary Claim: 1 No Drawings DRWN LN.CNT 769 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Compounds of the following general formula are useful in inducing an AB estrogenic response in a patient in need thereof: ##STR1## wherein R is -- CHO or -- CH. sub.2 OR. sub.1; each of R. sub.1 and R. sub.2 is hydrogen, alkylcarbonyl wherein the alkyl moiety has from 1 to 20 carbon atoms and is straight or branched, benzoyl, phenylalkylcarbonyl wherein the alkyl moiety has from 1 to 6 carbon atoms and is straight or branched or cycloalkylcarbonyl wherein the cycloalkyl moiety has from 5 to 10 carbon atoms; R.sub.3 is hydrogen; or R.sub.2 and R.sub.3 together form a double bond between the 17-position carbon atom and the oxygen atom. PΤ US 4078060 19780307 . in women, when they are generally admixed with a progestogen, SUMM hormonal support of menopausal and post-menopausal women including treatment of osteoporosis, treatment of acne in men and women, slowing down male pattern baldness in men and women, treatment of atrophic vaginitis,. . . be set against the undoubted benefits

resulting from their use. For example, diethylstilbestrol, a once widely used and well established estrogen has been implicated as possibly being responsible for vaginal cancer and adenosis in the female offspring of pregnant women treated. . . in humans and domestic animals in need thereof which will be substantially free of the undesirable side effects associated with estrogen therapy. . . . inducing an estrogenic response in a patient in need thereof

with lowered incidence of side effects that commonly occur with

SUMM

estrogen therapy and particularly with lowered incidence of side effects upon the blood clotting systems and the uterus. In essence the. . prevention of post-partum breast enlargement, acne, aging skin, male pattern baldness, contraception in conjunction with a progestogen for ovulation suppression, osteoporosis, benign prostatic hypertrophy, hirsutism, micromastia, chemical caponization of poultry, suppression of estrus in the bitch and growth promotion in cattle. SUMM . . . of the skin, particularly exposed facial skin and a thinning of the epidermis and loss of rete ridges, and post-menopausal osteoporosis or osteopenia. . . . amounts will provide a method of treatment wherein the SUMM potential for the occurrence of thrombotic effects is less than with estrogen treatment. The data contained in the following Table II indicate that 3,17-dioxoandrost-4-en-19-al does not bind in vitro with the

SUMM estrogen receptor of uterine estrogen target tissue. This binding is the first step necessary for hormonal action. To obtain these data female hamsters were ovariectomized. .

TABLE II SUMM

Uterine Cytosol Affinity Relative Estrogen Treatment Binding Affinity Estradiol 100 Estrone 22 Estriol 10 3,17-Dioxoandrost-4-en-19-al 0.01

The lack of estrogen binding affinity of 3,17-dioxoandrost-4-SUMM en-19-al supports the finding of lack of certain estrogenic side effects of the compounds employed in the. . .

```
ANSWER 183 OF 189 USPATFULL on STN
L4
AN
      78:6192 USPATFULL
      Pharmaceutical preparation adapted for oral administration
ΤI
      van der Vies, Johannes, Oss, Netherlands
IN
      Akzona Incorporated, Asheville, NC, United States (U.S. corporation)
PA
      US 4071623
                               19780131
PΙ
                               19760517 (5)
ΑI
      US 1976-687267
      NL 1975-6407
                           19750530
PRAI
      Utility
DT
      Granted
FS
EXNAM Primary Examiner: Roberts, Elbert L.
      Falk, Robert H., Wendel, Charles A., Young, Francis W.
LREP
CLMN
      Number of Claims: 32
      Exemplary Claim: 1,11
ECL
DRWN
      No Drawings
LN.CNT 533
      The invention relates to a novel pharmaceutical preparation with
AB
      oestrogenic activity adapted for oral administration comprising an
      oestradiol-17.beta.-ester, the ester group of which has been derived
      from aliphatic carboxylic acids having 9-16 carbon atoms, in combination
      with a non-steroidal lipoid. The preparation may additionally contain a
      progestational steroid or an androgen. The invention also relates to
      novel oestradiol-17.beta.-esters.
PΙ
      US 4071623
                               19780131
         . . produce restitution of the hormonal balance to such an extent
SUMM
      that in addition to other positive effects on body functions,
      osteoporosis in particular is checked. (See in this connexion,
```

for example, the article by J. C. Gallagher and B. E. C.. . .

```
CLM
       What is claimed is:
       10. A process for conducting estrogen deficiency therapy in a
       female patient requiring such therapy comprising orally administering
       daily to said patient from 0.001 to 2. .
     ANSWER 184 OF 189 USPATFULL on STN
L4
       76:30722 USPATFULL
AN
       3,17,18-Trihydroxy-1,3,5(10)-estratrienes
ΤI
       Engel, Klaus, Berlin, Germany, Federal Republic of
IN
       Prezewowsky, Klaus, Berlin, Germany, Federal Republic of
       Laurent, Henry, Berlin, Germany, Federal Republic of
       Nishino, Yukishige, Berlin, Germany, Federal Republic of
       Schering Aktiengesellschaft, Berin & Bergkamen, Germany, Federal
PA
       Republic of (non-U.S. corporation)
                                                                     <--
       US 3960841
                               19760601
PΙ
       US 1974-487969
                               19740712 (5)
AΙ
       DE 1973-2336432
                           19730713
PRAI
DT
       Utility
       Granted
EXNAM Primary Examiner: Love, Ethel G.
       Millen, Raptes & White
LREP
       Number of Claims: 17
CLMN
       Exemplary Claim: 1
ECL
DRWN
       No Drawings
LN.CNT 535
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       3,17,18-Trihydroxy-1,3,5(10)-estratrienes of the formula ##SPC1##
AB
       Wherein R is H or substituted or unsubstituted saturated or unsaturated
       hydrocarbon, and esters and ethers thereof, possess strong vaginotropic
       and only weak utertropic activity and are useful in the treatment of
       estrogenic deficiency conditions where uteral effects are not desired.
       US 3960841
                               19760601
PΙ
             . a favorable dissociated pharmacological activity, viz.,
SUMM
       strongly vaginotropic and weakly uterotropic activity, and are thus
       suitable for the treatment of estrogen deficiency indications
       where an estrogenic effect on the vaginal epithelium is desired, but an
       estrogenic effect on the uterus is. . . of estrogenic deficiency in
       postmenopausal females. Thus, the compounds are useful to delay the
       aging syndrome in such females, e.g., osteoporosis; depressive
       mood, peripheric circulatory disorders, cardiac diseases and senile
       otosclerosis.
     ANSWER 185 OF 189 USPATFULL on STN
Ļ4
       76:21792 USPATFULL
AN
       1,3-Oxygenated 8.alpha.-estratrienes
TI
       Prezewowsky, Klaus, Berlin, Germany, Federal Republic of
IN
       Laurent, Henry, Berlin, Germany, Federal Republic of
       Hofmeister, Helmut, Berlin, Germany, Federal Republic of
       Wiechert, Rudolf, Berlin, Germany, Federal Republic of
       Neumann, Friedmund, Berlin, Germany, Federal Republic of
       Nishino, Yukishige, Berlin, Germany, Federal Republic of
       Schering Aktiengesellschaft, Berlin & Bergkamen, Germany, Federal
PA
       Republic of (non-U.S. corporation)
                               19760420
                                                                     <---
PΙ
       US 3951959
                               19740712 (5)
       US 1974-488058
ΑI
       Utility
DT
       Granted
FS
EXNAM Primary Examiner: Roberts, Elbert L.
LREP
       Millen, Raptes & White
       Number of Claims: 24
CLMN
ECL
       Exemplary Claim: 1
```

DRWN No Drawings LN.CNT 771 8.alpha.-Estratrienes of the formula ##SPC1## AR Wherein R is lower alkyl and X is an oxygen atom, a .beta.-hydroxy or .beta.-hydroxy-.alpha.-substituted or unsubstituted saturated or unsaturated hydrocarbon group, and the esters and ethers thereof, possess strong vaginotropic but only weak utertropic activity and are useful in the treatment of estrogenic deficiency conditions where uteral effects are not desired. 19760420 PΙ US 3951959 . . an advantageous dissociated pharmacological activity, viz., SUMM strongly vaginotropic and weakly uterotropic effectiveness, they are preferably suitable for the treatment of estrogen deficiency where an estrogenic effect on the vaginal epithelium is desired, but an estrogenic effect on the uterus is to. . . the treatment of females in the postmenopausal period, e.g., climacteric and its sequelae, deficiency symptoms following ovarectomy and radiological castration, osteoporosis, depressive mood, perpheric circulatory disorders, cardiac diseases and senile otosclerosis. ANSWER 186 OF 189 USPATFULL on STN T.4 AN 75:10177 USPATFULL 17Alpha-ethynylestriol 3-Cyclopentyl ether TI Kraay, Russell J., Indianapolis, IN, United States TNFarkas, Eugene, Indianapolis, IN, United States Eli Lilly and Company, Indianapolis, IN, United States (U.S. PA corporation) <--19750225 US 3868452 PΙ 19731101 (5) US 1973-411988 ΑI Division of Ser. No. US 1971-136671, filed on 23 Apr 1971, now patented, RLI Pat. No. US 3790605 which is a continuation-in-part of Ser. No. US 1971-127690, filed on 24 Mar 1971, now abandoned DTUtility FS Granted EXNAM Primary Examiner: French, Henry A. Rowe, James L., Smith, Everet F. LREP Number of Claims: 2 CLMN Exemplary Claim: 1 ECL 3 Drawing Figure(s); 3 Drawing Page(s) DRWN LN.CNT 330 CAS INDEXING IS AVAILABLE FOR THIS PATENT. 17.alpha.-Ethynylestriol 3-cyclopentyl ether, estrogenic hormone useful in treatment of menopausal syndrome and all other conditions of estrogen deficiency or in which estrogens may be used therapeutically. <--19750225 US 3868452 PΙ 17.alpha.-Ethynylestriol 3-cyclopentyl ether, estrogenic hormone useful AB in treatment of menopausal syndrome and all other conditions of estrogen deficiency or in which estrogens may be used therapeutically. Estriol, a weak estrogen, has been used to treat menopausal SUMM syndrome because, unlike other estrogens, it has a relatively greater

SUMM Estriol, a weak estrogen, has been used to treat menopausal syndrome because, unlike other estrogens, it has a relatively greater action on the vagina. . . in preference to estriol itself because of their greater activity and oral efficacy. Quinestradol, however, is still an extremely weak estrogen compared to estradiol or 17.alpha.-ethynylestradiol. Quinestrol, on the other hand, is similar to other estradiol derivatives in that it causes. . .

The above compound is a potent **estrogen** having a favorable uterotropic-vaginal ratio in its hormonal action and, in a second aspect of this invention, there is provided a method of treating menopausal syndrome, either spontaneous or induced, as well as any other

estrogen-deficiency condition utilizing the above compound as the active agent.

As previously stated, 17.alpha.-ethynylestriol 3-cyclopentyl ether is a DETD potent estrogen having a favorable uterotropic-vaginal ratio in its hormonal action. The estrogenic activity of the compound is surprisingly high as measured. . .

. the vagina. It has been demonstrated by Jensen et al., Steroids DETD 13, 417-427 (1969) that the binding capacity of the estrogen binding protein of the cytoplasm is reduced after the rat is treated with estrogen. This reduction in binding capacity is significantly lowered at 4 hours after estrogen administration and generally returns to pretreatment levels at 24 hours. Clark et al., Biochimica et Biophysica Acta 192, 508-515 (1969) reported a simple convenient method to determine the amount of estrogen binding protein in the cytoplasm by utilizing the adhesive properties of the

protein after it had bound estradiol.

. . radioactive estradiol bound in vitro by the cytoplasmic DETD fraction is an indication that the tissue had previously been exposed to estrogen which reduced the binding capacity of the estrogen binding protein. FIG. 3 shows the results of the above experiment using estradiol or 17.alpha.-ethynylestriol 3-cyclopentyl . . the vagina while not acting on the ether. The narrow solid. uterus. By contrast, estradiol depleted both uterine (curve 3-C) and vaginal (curve 3-D) estrogen binding protein by about the same amount.

In employing 17.alpha.-ethynylestriol 3-cyclopentyl ether for treatment DETD of estrogen-deficiency conditions, particularly spontaneous or induced menopausal syndrome, a dose which provides on the average from 5 to 500 mcg. per.

The chief estrogen-deficiency state which 17.alpha.-DETD ethynylestriol 3-cyclopentyl ether is useful in treating is menopausal syndrome, either spontaneous or induced. Included in the term. symptoms: hot flashes, nervous irritability, depression, nocturnal sweating, leukoplakia, senile colpitis, vaginal kraurosis, kraurosis of the vulva, pruritus vulvae, post-menopausal osteoporosis and premature menopausal arteriosclerosis. Other similar estrogen -deficiency conditions, either natural or induced, can also be treated by the process of this invention.

TABLE 3 DETD

INTERACTION OF ESTRADIOL AND 17.alpha.-ETHYNYLESTRIOL 3-CYCLOPENTYL

WITH UTERINE AND VAGINAL ESTROGEN RECEPTORS

CPM/ml Cytoplasmic Fraction

Time After Administration (Hours)

Dose 0

24

48

SC Uterus

Vagina

Uterus

Vagina

Uterus

Vagina

CLM What is claimed is:

1. The method of treating estrogen deficiency symptoms in mammals which comprises administering an average of from 5 to 500 .mu.g. per day of 17.alpha.-ethynylestriol 3-cyclopentyl.

- L4ANSWER 187 OF 189 USPATFULL on STN
- 72:35186 USPATFULL AN
- 2-(1-HYDROXYALKYLIDENE)-3-OXO STEROIDS TI
- Clinton, Raymond O., New York, NY, United States IN

```
Sterling Drug Inc., New York, NY, United States
PA
                                                                     <--
PΙ
       US 3676426
                               19720711
ΑI
       US 1968-778345
                               19681122 (4)
       Continuation-in-part of Ser. No. US 1959-793292, filed on 16 Feb 1959
RLI
       which is a continuation-in-part of Ser. No. US 1958-723148, filed on 24
       Mar 1958, now abandoned
       Utility
DT
FS
       Granted
EXNAM Primary Examiner: French, Henry A.
       Lawson; Elmer J., Wyatt; B. Woodrow, Johnson; Thomas L., Bair; Robert
LREP
       K., Bourgeois; R. Clifford, Webb; William G., Wolfe; Roger T.
       Number of Claims: 18
CLMN
       No Drawings
DRWN
IN.CNT 1910
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Steroido[3.2-c]pyrazoles, having endocrinological, including anabolic,
       activities, are prepared by interacting 2-(1-hydroxyalkylidene)-3-oxo
       steroids with hydrazine or a substituted hydrazine. The intermediate
       2-(1-hydroxyalkylidene)-3-oxo steroids are in turn prepared by
       interacting a 3-oxo steroid with a lower-alkyl lower-alkanoate in the
       presence of a strong base.
       US 3676426
                               19720711
PΙ
       . . . are useful in the treatment of conditions arising from poor
SUMM
       nitrogen utilization; various debilitating diseases; bone conditions
       such as fractures, osteoporosis, osteogenesis imperfecta;
       degenerative joint diseases; traumatic injuries which bring about losses
       of large amounts of nitrogen, such as severe burns;. . .
       . . . interstitial cell-stimulating hormones. The pituitary
SUMM
       inhibiting properties were determined by standard test procedures
       involving a measure of the modification of estrogen-induced
       endocrinopathies upon parenteral administration in male rats [Beyler et
       al., Endocrinology, 58, 471-6 (1956)].
       2-Hydroxymethylene-17.alpha.-methylandrostan-17.beta.-ol-3-one was found
DETD
       to possess significant pituitary inhibitory activity as measured by the
       enhancement of estrogen induced testicular atrophy in rats at
       dose levels of 10-20 mg./kg./day.
     ANSWER 188 OF 189 USPATFULL on STN
L4
       71:48016 USPATFULL
AN
       PHARMACEUTICAL COMPOSITIONS COMPRISING 72-METHYL ESTRONE AND METHODS FOR
ΤI
       USING SAME
       Babcock, John C., Kalamazoo, MI, United States
IN
       Campbell, J. Allan, Kalamazoo, MI, United States
       The Upjohn Company, Kalamazoo, MI, United States
PA
                                                                     <---
       US 3627894
                               19711214
PΤ
       US 1967-666488
                               19670908 (4)
ΑI
       Continuation-in-part of Ser. No. US 1961-114621, filed on 5 Jun 1961,
RLI
       now patented, Pat. No. US 3341557 Continuation-in-part of Ser. No. US
       1960-69557, filed on 6 Nov 1960, now abandoned
DT
       Utility
       Granted
FS
EXNAM Primary Examiner: Roberts, Elbert L.
       Cheesman; Willard L., Kekich; John
LREP
CLMN
       Number of Claims: 4
DRWN
       No Drawings
LN.CNT 582
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       US 3627894
                               19711214
PΤ
       . . . inhibiting gonadatropin secretion, producing anabolic response,
SUMM
       especially in providing nitrogen retention, and in supplying calcium
       lost as a result of osteoporosis. In addition, the compounds
       of formula II, when combined with progestins such as
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6.alpha.-methyl-17.alpha.-hydroxyprogesterone 17-acetate (Provera), 7.alpha.-methyl-17.alpha.-ethylnyl-19-nortestosterone, 17.alpha.-hydroxy-6-methyl-16-methylene-4,6-pregnadiene-3,20-dione 17-acetate (Melengestrol. . acetate), etc., are useful for the prevention of ovulation in DETD mammals. Administration to mammals depends on the particular progestin and estrogen involved and the individual's response thereto. In general, a dose of between about 0.01 mg. to about 5 mg. of. L4ANSWER 189 OF 189 USPATFULL on STN AN 71:46562 USPATFULL COMPOSITIONS COMPRISING 7.alpha.-METHYL-17.alpha.-LKYLATED ESTRADIOLS ТT Babcock, John C., Kalamazoo, MI, United States IN Campbell, J. Allan, Kalamazoo, MI, United States The Upjohn Company, Kalamazoo, MI, United States PA 19711207 US 3626061 PΙ 19670908 (4) ΑI US 1967-666466 Continuation-in-part of Ser. No. US 1961-114621, filed on 5 Jun 1961, RLI now patented, Pat. No. US 3341557 Continuation-in-part of Ser. No. US 1960-69557, filed on 6 Nov 1960, now abandoned DTUtility Granted FS EXNAM Primary Examiner: Roberts, Elbert L. Cheesman; Willard L., Kekich; John LREP Number of Claims: 6 CLMN No Drawings DRWN LN.CNT 1091 This invention relates to novel 7.alpha.-methyl-17.alpha.-alkylated AΒ estradiols and processes for their preparation; more particularly to those compounds embraced by the formula (11) ##SPC1## Wherein R is selected from the group consisting of hydrogen, the acyl radical of a hydrocarbon carboxylic acid containing from one through 12 carbon atoms, an alkyl radical containing from one through 8 carbon atoms, tetrahydrofuranyl, tetrahydropyranyl, 5-substituted tetrahydropyranyl, and a silyl ##SPC2## Selected from the group consisting of alkyl of one through eight carbon atoms and phenyl, R' is selected from the group consisting of hydrogen, methyl, ethyl and 1-propynyl, and R" is selected from the group consisting of hydrogen, the acyl radical of a hydrocarbon carboxylic acid containing from one through 12 carbon atoms, and a silyl radical of the formula ##SPC3## It also relates to 7.alpha.-methyl-17.alpha.-alkenylestradiols (11a) and their preparation. <--19711207 US 3626061 PI. inhibiting gonadotropin secretion, producing anabolic response, SUMM especially in providing nitrogen retention, and in supplying calcium lost as a result of osteoporosis. In addition, the compounds of formula II, when combined with progestins such as 6.alpha.-methyl-17.alpha.-hydroxyprogesterone 17-acetate (Provers), 7.alpha.-methyl-17.alpha.-ethynyl-19-nortestosterone, 17.alpha.-hydroxy-6-methyl-16-methylene-4,6-pregnadiene-3,20-dione 17-acetate (Melengestrol. . acetate), etc., are useful for the prevention of ovulation in DETD mammals. Administration to mammals depends on the particular progestin and estrogen involved and the individuals response thereto. In

general, a dose of between about 0.01 mg. to about 5 mg. of.